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ON
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BY
ADOLPH RUPP, M. D.



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Remarks on Antitoxin, Diphtheria, the Practitioner, and History

Reprint from the MEDICAL RECORD, November 5, 1898

A Practical View of Antitoxin and Diphtheria in Private Practice

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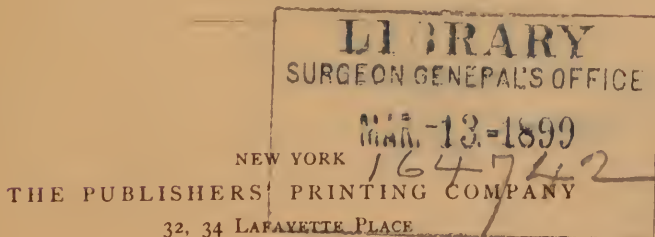
Antitoxin, Diphtheria, and Statistics

Reprint from the MEDICAL RECORD, January 28, 1899

BY

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“However unwillingly a person, who has a strong opinion, may admit the possibility that his opinion may be false, he ought to be moved by the consideration that however true it may be, if it is not fully, frequently, and fearlessly discussed, it will be held as a dead dogma, not as a living truth.”—JOHN STUART MILL.

“Erfahrungen wie Einsichten sind neue Prüfungen, geben zu neuen Zweifeln Anlass.”

—J. G. HAMANN.

“Experience and insight are experiments which arouse our doubts anew.”

“A writer who endeavors to penetrate beyond the surface of things, though he may be sometimes too minute, and, at others, even erroneous, will, however, clear the way for succeeding adventurers; and, perhaps, make even his errors subservient to the investigation of truth.”

—OLIVER GOLDSMITH.

REMARKS ON ANTITOXIN, DIPHTHERIA, THE PRACTITIONER, AND HISTORY.

By ADOLPH RUPP, M.D.,

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WHEN diphtheria antitoxin was supposed to be obtainable in that degree of perfection which seemed to justify laboratory workers or scientists, in their own estimation, in proclaiming it a scientific product of surprisingly great curative value, it was forced rather than argued into the hands of practitioners. The force exerted was not that of legislative action, but that of public opinion. This opinion was created and developed by the influential voices and pens of many prominent scientists and clinicians, and not the least by the lay or political press. The amount and extent of hopeful expectancy thus aroused generally among practitioners and the laity made it extremely impolitic for most practitioners to entertain, and much more so to practise, views and convictions of their own not in accord with the teachings of Behring and Roux and others. The jubilations of some practitioners amounted to—in some instances do so still—claims of infallibility for the remedy and their own individual wisdom. Those who did not and do not think and do as they think and do, they accused and accuse of dulness, even of crime. These enthusiasts always meant and mean well. Infallible people always mean well.

Concerning the use of antitoxin as a remedy in individual cases of diphtheria, the practitioner has rights as well as duties to urge him on. It is not a

question of right only or of duty alone, but of both duty and right. He deals not only with cases of disease; he deals with his patient and the patient's friends. And his first-all-around duty is to do all the good he can, and, if possible, no harm of any kind. In doing so it is not necessary for him to be either a tyrant who must have unquestioning submission, or a martyr who fails to have his will recognized and applauded. It is also a duty of his to give observations and facts, opinions and fancies, considerate attention and study, even though such do not fall in graciously with his own observations and with facts as he sees them, etc. But it is his right to trust his own senses and his own reasoning powers. In attending to his duties, and in generously maintaining his rights, he should be actuated by a modesty and objectivity that will leave him too proud to be vain and wise above his stature.

After observation and experimentation have done all they can to give us facts we are obliged to build up ideas with our facts. Our facts are useless unless something is made of them. But facts are odd things and hard to understand sometimes. To some people a fact is valid because some influential person claims it to be fact. Others would call "a fact" anything that can gain the assent of a majority of competent judges. Thus, to gain a fact a minority of competent judges is pushed aside, and satisfaction is got. Facts of this kind have been abundantly accumulated on the doings of antitoxin in diphtheria. History teaches over and over again that neither a great name, nor a majority of great names, necessarily determines the reality and validity of fact definitely, or once for all. Great names demand attention, and a unanimity of many great names demands from us a greater amount of attention and consideration. But great names should not command submission and self-abnegation. Neither do minorities monopolize all wisdom. Mi-

norities often go wrong no matter how select their make-up may be. The wrong interpretation of facts, so-called, on the one hand is due to incomplete or partial perceptions, and, on the other, is made when much preconception or theory has been projected into the fact which is really not justified in being there. Diphtheria is a fact, and so is antitoxin. But both these single words comprehend not a single fact, but in many respects a rather intricate mass of fact and theory which is struggling into a final disentanglement and definition. The simple eloquence of some writers and debaters who glibly use these words—diphtheria and antitoxin—is as charming as it is illusory. They use substantialized abstractions that have no real properties. They refuse to argue. They are sure of their fact, and they feel that they need not analyze it. Men of genius and extraordinary talent have erred in this respect. The unknown elements that are a part of all facts—like the ashes of chemical analyses—are lightly thought of. It took nearly a half-century of hard laboratory work and fervid discussion finally to demonstrate that Liebig was not altogether wrong and Pasteur not altogether right concerning the facts of bacteria and fermentation.

Although many able practitioners and scientists claim that antitoxin for diphtheria has ceased to be a question, and that all argument concerning the fact of its utility is futile labor, other equally able observers and equally well-equipped practitioners claim that it is a fact that the remedy is useless and at times harmful.

Whatever the inclinations and tastes of practitioners may be concerning the contentions of opposing authorities, they have three sources open to themselves from which to gather facts and opinions for justifying their own ways of thinking and practice: 1, history; 2, laboratory reports; 3, clinical experience.

I do not purpose to deal in this paper with either

the laboratory aspect or particularly with the clinical character, quantities, and facts of diphtheria-antitoxin questions. All that is intended now is to direct attention to what may be called the historical or traditional conception of diphtheria, and in a way to compare it with present-day notions. We may thus get rid of some misconceptions and attain to some certainty of meaning, of definition, and, to a certain degree at least, be enabled thereby to judge—for we all must finally judge in these matters—to what extent, if at all, we may or may not be justified in accepting what some authorities claim for antitoxin in the treatment of diphtheria. All definitions are something more than a mere statement or epitome of leading facts. They also imply theories concerning the facts. The bare facts are unchanging. The theories, the explanations, are tentative only. Looking at the history of diphtheria reveals to us that the interpretation of the phenomena of this disease resolves itself into a dissolving conception, which for a time again solidifies into a fixed and standard conception. The facts, the phenomena of diphtheria we are always willing enough to believe to be true; and the will to believe is often stronger than the energizing theory.

What is diphtheria supposed just now to be? It is defined as being an acute infectious disease. It was always considered to be that. But our modern teachers—many if not all—supplement their definition and statement of leading facts with a theory. They say that diphtheria is caused and developed by the growth of a specific bacillary organism. This specific bacillary organism is a revolutionist. It has changed and modified the concept of this disease. The bacillus claims almost undivided attention. We knew in days before the bacillus was pilloried that diphtheria was chiefly and generally limited to the upper respiratory tract. We also knew that abraded surfaces of the skin sometimes became affected with membranous de-

posits. In the present day we are taught that the disease first appears as a local disorder. This local disease is characterized by inflammation and a false membranous deposit. This was not the generally accepted doctrine in prebacillary days. The disease was supposed to be primarily constitutional. Whether it be considered primarily constitutional or primarily local, much theory goes mixed with the facts. There is such a condition as a predisposition—the constitutional or organic condition that makes the specific cause a possible rioter—a successful cause and developer of disease. To-day our teachers say that the system is secondarily affected—a general disease is produced which is a consequence of the local one. Older and antibacillary theories made the facts consort the other way. First came blood changes, and then local manifestations developed. And yet even before bacilli became important facts in our reasonings, some observers had leaned toward an impression that diphtheria is first a local disease and then a constitutional trouble. In days gone by the eye made the diagnosis. An inflamed throat with peculiar patches on the pharynx, palate, or tonsils, or on all three together, in connection with constitutional symptoms more or less marked, justified a diagnosis of diphtheria. Bretonneau had stated that when there was no pseudo-membrane there was no diphtheria. From this type—from mild cases to severe ones—the variations have been, since the days of Bretonneau, very considerable. The chief factors giving rise to the variations from a mild type are enveloped in such notions as that epidemic influences hover in the air or are secreted in the earth. Individual predisposition is another factor. In times gone by much stress has been laid on these factors in giving definition and clearness to the diagnosis of diphtheria. Older physicians also noticed that diphtheria was sometimes complicated by gangrenous and septic processes. They had observed too that the constitu-

tional symptoms were sometimes grave, out of all proportion to the local signs; and the obverse was sometimes the case. But in whatever manner the local and constitutional conditions consorted, as to character and degree, epidemically or individually expressed, the diagnosis was determined by the pseudo-membranous deposit. No deposit, no diphtheria. All the records of this disease, from Bretonneau to Behring and Roux, are based on this conception of diphtheria—a disease which varies from a benignity so mild as to escape attention to a malignancy which is as disgusting as it is disheartening. The conception was not formed in the course of a single epidemic, or in the course of a single endemic cycle; it is the result of centuries of observation and correction, and is the final entity of thought and being resulting from dissolving contradictions of all kinds which make up the natural phenomena of a disease and the phenomenon of the concept of that disease as it establishes itself in the minds of successive generations of men.

The modern definition of diphtheria differs very much from the historical definition as it existed up to five or ten years ago. Laboratory scientists, who more or less rigidly fix conditions to fit what they hope to prove, get a disease which they call diphtheria. Accepting all their preconceptions, and the conditions they surround them with, the result of their labors and cogitations must necessarily be accepted as being logical. But logic is only method; logic is not nature. Nature, too, is logical, but on a broader basis than can be found in our laboratories at the present time. Our scientists, and those who aspire to compel us to concur in their notions of exceptional exactitude, tell us that we have diphtheria when we have a sore throat in which the Klebs-Loeffler bacillus is found. The bacillus and the sore throat settle the diagnosis. The presence of a pseudo-membrane is of

secondary importance only in so far as diagnosis making is concerned. The membrane may or may not be diphtheritic. This conception of diphtheria is clinically inadequate. It does very well for the laboratory. In the laboratory excellent results are obtained by treatment with antitoxin. We clinicians cannot but admit that these laboratory observations, experiments, and successes have added a factor to our conception of what diphtheria is. The factor is the Klebs-Loeffler bacillus. This minute factor also carries a good deal of theory with it, which is too often accepted as fact. Henle used to say that a theory is to be valued not so much by what it can prove, as by how much or how little it assumes. The scientist theory proves everything and demonstrates only a modicum, and leaves a good deal unaccounted for which it lets shift for itself. The scientist overlooks the importance of the historical conception of diphtheria—and he overlooks the importance of other bacilli at work in the local uproar. Neither oversight acts kindly toward the theories of specific antitoxin therapeutics, either in the specific and limited methods of logic characteristic of laboratory workers, or in a practical demonstrative way.

From a study of definitions or conceptions—the historical or traditional, and the scientific or laboratory conceptions—we may conclude, and properly so, that they are, taking everything into consideration, unlike, although similar in a few respects; and it must follow as surely as the day the night that what will cure in the one case cannot cure in the other, except perhaps in such a limited way as the few points of similarity may justify or give hope for. Furthermore, when the results of treatment of historical diphtheria are taken as a standard for showing off the superior virtues of antitoxin in the treatment of modern or laboratory diphtheria fallacies are committed. How great the contrast becomes when we change our methods of

diagnosis because we change our conceptions of a historical disease is glaringly illustrated by Dr. McCallom, of the health department of Boston. His figures are no doubt honest and scientific. He tells us that from 1891 to 1894—a period of four years—ten hundred and sixty-two cases of diphtheria were reported. These cases were diagnosticated by the eye and by other traditional methods. But from the 1st of September, 1895, to the 1st of October, 1896, nineteen hundred and seventy-two cases of diphtheria were reported. He explains this great increase thus: “The number of cases of diphtheria reported was largely increased on account of the larger number discovered among the pupils of the public schools, by the medical inspectors of the schools, and the bacteriological tests in the otherwise unrecognized cases.” Thus laboratory methods discover the disease which eluded the eye. This may be bacillary diphtheria, but it is not diphtheria in the historical sense. It is not the diphtheria in the old clinical sense. In contrasting these nineteen hundred and seventy-two cases of bacillary diphtheria, collected within a period of thirteen months, with the ten hundred and sixty-two of clinical diphtheria observed in four years unlike things are contrasted. The difference is almost as great as between eight and one. He gives the rate of mortality of diphtheria diagnosed by old methods as being forty-five per cent. The rate of mortality of bacillary diphtheria—that is, the diphtheria diagnosed in the laboratory on scientific principles—is thirteen per cent. What do these percentages prove? Dr. McCallom naively claims in his report that they prove the beneficent curative qualities of antitoxin. They do nothing of the kind. Not only are unlike things contrasted, but, if his contrast is allowed to pass as a comparison, he conveniently fails to credit the four years’ collection of diphtheria with the proportion of cases that were not recognized because school inspectors and bacteri-

ological tests were not on the track of the bacillus. According to Dr. McCallom's figures, clinical diphtheria falls in point of frequency about eight points from a standard of one which is the Boston, or scientific diphtheria. All other things concerned in the comparison fall in a like manner proportionately. Thus, if all things are taken on a basis of equality, historical or clinical diphtheria is, according to Dr. McCallom's honest figures, seven times less frequent than that of the health department of Boston, or scientific diphtheria. Science so-called has done this much—it has increased the figures of an old disease sevenfold. But what science means, and what clinical observation has meant, are two different things. The scientific inflation deals with new definitions which do not cover the older ones, and, comparing these exaggerated figures—exaggerated in comparison with those obtained by traditional methods—they can only be said to have a nominal, but not a real relevancy. If the scientific methods (Dr. McCallom's) of obtaining a superior death-rate percentage were equal to the scientific methods of increasing the numerical morbidity, then Dr. McCallom's death rate ought to be about five or six per cent. and not thirteen per cent. And then *the* argument in favor of antitoxin would not be remarkable, or even worth serious attention. Dr. McCallom has confounded elementary conceptions, unlike in kind, and has arrived at results that are unlikely.

In a subsequent essay I shall discuss the practical arguments and supposed facts which some clinicians and scientists claim do prove that antitoxin is the remedy for diphtheria. Aside from all speculative and theoretical considerations, and dissimilarities of definition, these practical arguments and proofs resolve themselves into an enumeration of authorities and cases.

A PRACTICAL VIEW OF ANTITOXIN AND DIPHThERIA IN PRIVATE PRACTICE.

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ANTITOXIN is the name given to a laboratory product, the essential nature of which is pathological. Its measurements of therapeutical values or units are of an arbitrary character, uncertain, and unequal. These units of therapeutical valuation are not exact, but approximate biological appreciations, translated from zoological probabilities into anthropomorphic possibilities. And the unit of value is as variable as the element of individual resistance at both ends of the animal scale where the tests apply. There can be no absolute or fixed standard of measurement. It is a question of more or less. Its chemical composition is unknown, and its physiological action is yet to be determined. We know that it is a poison from its effects on the animal economy. Many experimenters and clinicians claim that it inhibits, counteracts, or neutralizes the action of the poison of diphtheria which develops in the animal and human body. Antitoxin is a word that scientists may well claim as their own. It had its birth in the laboratory. Diphtheria, however, is a word that is not the sole property of scientists. Clinicians have used the word diphtheria in an empirical sort of way for years and years, to designate a condition characterized by more or less constitutional disturbance and an inflamed sore throat, accompanied at the same time by depositions of pseudo-membrane. "No membrane, no diphtheria," was the keynote.

In 1861 Alonzo Clark wrote: "There is some vague-

ness in the use of the term diphtheria. . . . While diphtheria prevails, it is usual to have at the same time a sore throat prevailing epidemically, which has but little tendency to the production of membrane. And as these two forms of disease are apt to go together, physicians have been somewhat in the habit of grouping them under one head and considering them both diphtheria." The habit, it should not be forgotten, was not general; it was only somewhat so, not generally so. Not only Clark, but many physicians besides, thought it necessary to separate these synchronous affections, because "the form of sore throat which is not attended by the production of membrane is a mild disease, and is almost never fatal."¹ "The very term diphtheria," he continued, "implies the existence of a false membrane; and we must limit the signification of the word to such inflammations as terminate in or have in their course this membrane as a sign." Clark goes on to say, "To make this membrane the basis of classification may not be scientific, but it is practical. And," he said correctly, "science requires us to make distinctions where there are differences. And here [between the benign sore throat and the diphtheria, as defined] we have the broad difference that one disease is ephemeral, with a tendency to recovery; and the other is often [not uniformly so] terribly fatal, and is liable to a long train of symptoms of a serious if not of an alarming character."

Clinically and historically we have a true diphtheria varying much in severity as individual cases come and go; and clinically and historically a false or pseudo-diphtheria, which is a mild disease and very rarely fatal. These terms in their historical and clinical senses are unlike the same terms used by scientific physicians and bacteriologists of our day—the terms in their historical meanings stand for different things, and are conceived of in different ways. And

¹ American Medical Times, March 23, 1861, p. 187.

yet in our day the terms and their meanings are very often confounded, and discussions consequently often result in confusion, and fallacies and misunderstandings are disseminated.

Scientists have given us the facts of the Klebs-Loeffler bacilli and other cocci to think of, and these low forms of life have dislocated our ideas of diphtheria, true and false. But scientists are not a unit as to the significance of the Klebs-Loeffler bacilli for diphtheria and its relationships to the other bacteria which are granted an active participation in the local processes of this clinical disease. Concerning their diagnosis of this disease as defined by themselves, scientists do not base their diagnosis on the number of Klebs-Loeffler bacilli that may be present, absolutely or comparatively, over against the number of other cocci and bacilli that may be present in clinically true or false diphtheria. The mere presence of the Klebs-Loeffler bacilli demonstrably qualifies their diagnosis. Incongruities of quantitative facts are readily explained away by such terms as mixed infections. When an apparently bad case of clinical diphtheria is met with and no Klebs-Loeffler bacilli are detected, we are assured that the case is false diphtheria. And if a case of clinical diphtheria develops a membrane that persists longer than one or two or three weeks, even though antitoxin has been given *lege artis*, and even though the Klebs-Loeffler bacilli are detected, the scientific diagnostician tells us that the case is one of mixed infection, and that the persistence of the membrane is due to various cocci and other bacteria than the Klebs-Loeffler form. To the scientist neither of these forms is true diphtheria.

We are assured by the scientific physician that "false diphtheria is a very dangerous disease, though its mortality is not as high as that due to the Klebs-Loeffler bacillus."¹ This is given us as a bare asser-

¹ "The Modern Treatment of Diphtheria, etc.," by Aug. Caillé. Reprint from the Post-Graduate, October, 1897. p. 3.

tion. We must accept it on faith and as a scientific definition. Notice the difference and the distinction made by practical physicians, as voiced by Clark about thirty-five years ago. It is a new revelation! Bacteria are ubiquitous. If we are to accept as fact the reports of all bacteriologists collectively that we can find time to read, we shall be obliged to conclude that no single kind of bacilli or cocci is found alone doing mischief. And if we accept the teachings of any one particular bacteriologist as telling the truth, the whole truth, and nothing but the truth, we shall find it easy enough to be logical, but we shall find ourselves differing much from the conclusions arrived at by others who pin their faith to the finds and teachings of some other one particular bacteriologist. For instance, Baumgarten claimed that streptococci are the true primary cause of diphtheria, they being always present in cases of clinical true diphtheria; and that the Klebs-Loeffler bacilli are only of secondary or accidental importance in this disease, because they are not invariably present. Baumgarten is no novice. He strengthened his contention by saying that streptococci are not found in healthy mouths and throats, but that Klebs-Loeffler bacilli are. And now comes Dr. Paul Hilbert, who tells us that although everybody must admit that Baumgarten is one of Germany's most eminent pathologists, yet he is wrong in what he has seen and in his contentions. Hilbert was successful in finding, in all cases examined by him, the specially reputed pathogenetic long streptococci in the crypts of tonsils of healthy people.¹ Streptococci are very convenient things to deal with. Nothing so obliging! They explain rheumatism for some scientists. In the estimation of others they generate acute suppurative tonsillitis, and skip

¹ "Die Rolle der Streptocokken bei der Diphtherie." Dr. Paul Hilbert, Verhandlungen des Congresses für innere Medicin, Sixteenth Congress, 1898.

away quickly for the benefit of the patient when staphylococci make up to push them out of sight. When suppuration of any kind or anywhere takes place, then they are there, active, obstreperous busy-bodies, to help the scientific logician. It is not at once easy to see how Caillé or any clinician can be sure that streptococcic diphtheria (or, rather, his and others' non-Klebs-Loeffler bacillary or false diphtheria) is less frequent in occurrence than Klebs-Loeffler diphtheria. Hilbert affirms that streptococci are usually around, and, if not immediately so, they are always close at the heels of Klebs-Loeffler bacilli in cases of scientific diphtheria anyhow.

Some things in this connection that a New York physician can be sure of, thanks to health-board bacteriologists, are:

1. Some, not by any means many, of his cases that run a course of true clinical diphtheria from start to finish are false diphtheria in the scientific sense, despite the presence of the pseudo-membrane.

2. Some of his cases, only occurring now and then at longer or shorter intervals, develop or show up the presence of the Klebs-Loeffler bacillus when all active local processes have become clinically a thing of the past.

3. In the great majority of his cases of clinically true diphtheria the Klebs-Loeffler bacillus is found. The health board gives only qualitative information. Other information than the Klebs-Loeffler presence is not furnished the practitioner, except when the Klebs-Loeffler bacillus is not found. Now if Hilbert is right in his contention, and Baumgarten in his, all these cases of true clinical diphtheria are cases of mixed infection—streptococcic, etc., and Klebs-Loeffler bacilli. Baumgarten's testimony in a large measure neutralizes Hilbert's. But it may be interesting to state here that one of the lessons that Hilbert tries to enforce is this: Streptococci alone are not so bad, but

when Klebs-Loeffler bacilli fall in with them, why then a bitter fight ensues, which can be checked by the early administration of antitoxin. After Klebs-Loeffler bacilli and streptococci have been damning and damaging the patient for a longer or shorter while, they create such havoc that antitoxin given late can do no good. Antitoxin early administered paralyzes the Klebs-Loeffler bacillus, and then streptococci give up the fight. They don't seem to be enamoured of a fight single-handed, as it were. Hilbert thus introduces a new element into the antitoxin controversy without clearing up the befogged questions.

The reader will please excuse the Hilbertian digression. New York physicians know from experience that few clinically true diphtherias are not also true scientific diphtherias. And according to my experience and practice, and according to the practice of many of the New York physicians known to me, very, very few cases of clinically false diphtherias are reported to the health board. The presence of a pseudo-membrane in the throat that is sore determines almost invariably the report of diphtheria to the health board. And this is so because the practitioner thinks clinically, and is obliged to do so, no matter how well informed he may be concerning science and statistics this way and that way.

From a clinical standpoint I have collected notes from over one hundred practitioners in and outside of this city on antitoxin and its value as a remedy in the treatment of diphtheria. My correspondents and acquaintances, like those who have written and parleyed on this subject, can be divided into three classes:

1. Those who positively affirm superlative results.
2. Those who are doubtful and undecided, but who use antitoxin.
3. Those who are sceptical and condemn its use theoretically, if not always practically.
 1. Six physicians in a hundred with whom I have

compared notes, one of them a homœopath, have not used antitoxin. These men may be prejudiced, but they are not cowards—they have the courage of their opinions. And in most of the practical concerns of life they prove to be as wise and able as the enthusiasts or doubters. All of them have seen antitoxin used, and observed the cases afterward. One of them affirms that in a case that he had treated the Klebs-Loeffler bacillus was not discovered until after antitoxin had been injected, and then the pseudo-membrane that had been undergoing dissolution became actively formative and spread. My homœopathic friend is sure that in a case of his which he refused to treat with antitoxin, but in which another physician administered the remedy on the third day of the disease—this patient died a few days afterward of “suppression of urine.” And prior to the administration of antitoxin, he claims there were no evidences that the child would die of such a complication. Another of these sceptics says that a patient, in which he had no power to prevent antitoxin from being used, died soon after of endocarditis.

2. My friends who doubt and are not sure one way or the other are as numerous, almost, as the enthusiasts. Statistical tables influence them only very little. One of these physicians, who had used this remedy faithfully in every case that came into his hands, summarized his view thus: “Either the whole theory is false, or else the best antitoxin we can get is worthless.” This man is no fool. Neither is he in a hurry to reach conclusions. His perceptions are quick, and he is a good diagnostician. Another of this class says he uses antitoxin when he may, and that he had seen patients die in which antitoxin was used, as though so much water had been injected. He, however, believes that antitoxin acts on the heart in an unpleasant way, accelerates the pulse, and increases the temperature for a time. In some cases he thought antitoxin acted

decidedly like a poison. He had one case of "fatal syncope and convulsions" follow a few hours after antitoxin had been injected. He gives antitoxin because public opinion obliges him to be up-to-date and scientific. On the whole, none of these men can see that antitoxin does any good in those cases where they would most wish to get beneficial effects. They have seen croup develop under its use. So far as their own experience goes, they are not able to see that other complications are rarer than before they used antitoxin.

3. If the enthusiasm of a good many honest men could settle the high reputation of any therapeutical remedy, then there would long since have ceased to be any question concerning the superlative value of antitoxin for diphtheria. My enthusiastic friends are enthusiasts! One of these friends wrote to me: "The evidence is so overwhelmingly in favor of antitoxin, and the advantages of the treatment are so well known and so frankly acknowledged, that any one who should attempt to write it down would stultify himself, unless he could produce evidence not yet known to literature and subversive of what we know, which is rather impossible." Such talk is typical. One hears the like rather often in New York. This distant friend had a syncopal case—made so, he admits, by a dose of antitoxin—which he came near losing. He also had an adult case of diphtheria in which the membrane persisted in the throat for weeks, although repeated doses of antitoxin had been given. Klebs-Loeffler bacilli were present in this case, but he says they were few and that the persistence of the membrane must have been due to streptococci. Streptococci act as an apology for the inefficiency of antitoxin under other circumstances and varying instances of mixed infection.

Another friend and enthusiast, practising in a Western country town, had used antitoxin for over one year when it first came out. Thinking that his results were no better than before, he gave up using it. Then his

losses of croup cases disheartened him, and he again used antitoxin. He now became more hopeful. He thought he was preventing croup, and that cases of croup that came his way were being saved, as was not the case before. But by the end of the year he was not satisfied with the totality of successes recorded, and he this time concluded that the antitoxin was not so good as it ought to have been. He wrote to the makers of the antitoxin that he had been using, giving them his views and experience. The firm replied, suggesting that his cases may have become worse, etc., and that their antitoxin was as good as could be obtained. He now tried another make. Again he was jubilant over his results. But strange are the workings of facts and fate! This last make, that was filling his heart with joy and thanksgiving, was doing worse in a distant city hospital than the antitoxin he had discarded. To this friend antitoxin is the greatest discovery of the century. He has not found it necessary to tracheotomize or intubate any of his croup cases since he has changed the make of antitoxin—that is, when used early enough, which in his experience is not the third, but the fifth day of the disease (diphtheria). It is not an uncommon thing for this class of men to excuse their lack of success with the plea that this or that brand or make of antitoxin was or is below the standard. One of my enthusiastic friends told me that in his experience any make or brand of antitoxin becomes less and less efficient after the fourth week of its making. It is not like good wine!

Another enthusiastic acquaintance, who has a large general practice and who holds both a homœopathic and a regular diploma, claims to have had cases of all sorts of diphtheria which he treated with antitoxin, and in upward of eighty of them with success; there were no deaths. And these successes he claims resulted from doses varying from six hundred to one

thousand units. Sometimes he had given larger doses. But he only rarely found it necessary to repeat the dose. Soon after this communication he had several deaths in rapid succession. On these I have had no comment from him.

Another of my enthusiastic friends, commenting to me on his fatal cases that had been treated with antitoxin, gave me to understand that they died, not of diphtheria, but of incidental complications—pneumonia, Schluck-pneumonia, and nervous troubles; never of croup *per se*.

So much from my friends; and now for my own personal experiences.

I have treated twenty-four of my diphtheria cases with antitoxin, and, I have the good fortune to be able and say, without a death or any very serious casualty resulting. Of course, other remedies and medicines formed part of the general treatment of these cases. The ages of these patients ranged between the second to the eighth year of life. I have given as large a single dose as twenty-five hundred units, and as small a one as six hundred units. No sign of any particularly marked character made itself evident to signify the difference of dosage in the different cases. Opinion, among my antitoxin acquaintances, differs as to the size or quantity of serum dosage necessary to obtain desirable and striking results. Some gave six hundred units and were satisfied. Others have been advancing the dose quantities, thus keeping abreast of advancing scientific recommendations. When smaller doses were given, the results were as favorable as they are now, in so far as can be gathered from their reports. These men have followed the recommendations of authorities and literature.

In most of my cases one injection of one thousand units was given on two successive days. In several, two injections were given on the same day. In a half-dozen cases one injection was given on three succes-

sive days; and in several others one injection on four successive days. In none of my cases were the immediate or after results such as to impress on my senses any of the reported magnificent effects vaunted by Baginsky and other enthusiasts.

Of these twenty-four cases, one, a boy, four years old, had to be tracheotomized; another, a girl of five, was intubated; and another, a girl of six, was also intubated. The tracheotomized boy was croupous when first seen, and was reported to have been sick only a few days. Fifteen hundred units of the health-board antitoxin was immediately injected, and six hours later another one thousand units. There was membrane in the nose and pharynx, not abundant; and the boy had a temperature of only 102° F., and was not very bad otherwise. But in spite of the antitoxin the croup progressed, and, intubation failing to give relief, he was tracheotomized, the membrane having extended into the trachea; the canula was removed eight days after operation. The membrane in the pharynx disappeared slowly and was gone five days after the operation had been done. This boy also received about eight hundred units the day after the operation. The relief obtained by tracheotomizing was marked and evident; but not so were the antitoxin effects.

The six-year-old girl when first seen was but slightly croupal, and was reported to have been sick but a day. I thought her illness of longer duration. I offered to administer antitoxin. The parents would not consent. Next morning she seemed better. The deposits on the tonsils had become less, but a thin streak of membrane was seen stretching downward behind the posterior pillar of the fauces on the left side. Again—the fifth day of illness according to my view—the antitoxin was spoken of. The parents now consented to have this new remedy given. Accordingly twelve hundred units was administered in the afternoon. No change had taken place, except that the membrane on the

tonsils seemed less, but that behind the faucial pillar had enlarged. Next morning—the sixth of the disease—the child was much more croupous, somewhat cyanotic, but not markedly so; the temperature had gone up from 100° to 102° F., and I had to speak of the possibilities of an operation—intubation. The father of the child then turned on me and said: “The child was much better before antitoxin was given.” We parleyed much, and operation was finally consented to. Operation became necessary on the evening of this, the sixth day of the disease. At my 10 P.M. call I noticed a hissing sound now and then when the child cried. I inferred that this sound was caused by air pressing up along the outside of the tube, and I put the child’s watchers on guard. I told them the tube might be coughed up. At the time the tube seemed effective and firmly in place. At 1 A.M. of the seventh day of illness I was called, and found that the tube had been coughed up. When I saw the child she was sleeping calmly. Her respiration was hissing, occasionally, but not obstructed; nor was there marked cyanosis. I let her alone, but watched her for several hours, and then went home. This girl developed an irregular and intermittent pulse. She finally recovered, but with a slight paralysis of the palate, which lasted several weeks.

The other five-year-old girl had one thousand units injected on the afternoon of the first day’s attendance. She had bronchitis. It was reported that no membrane was present in the morning. In the evening when I saw her her temperature was 103° F., and there were thin deposits on the tonsils. I gave her another injection—a little more than twelve hundred units—and then she was intubated next morning. At a later visit she was given one thousand units more of antitoxin. The membrane disappeared for the most part on the third day after intubation. This child could gargle. But here and there little flecks of membrane

persisted for two days longer. Thus in this case membrane persisted in the throat for five days after it was first noticed. The tube was removed on the seventh day after emplacement. This child had an intercurrent catarrhal pneumonia. Here, too, the heart condition that developed after the injection of antitoxin necessitated strychnine injections and alcoholic stimulation.

In none of these cases did antitoxin seem to have any inhibitory influence on the progressive croupal process; and in the three cases the membranous deposition was rapid, and in none of them did the antitoxin have any effect apparently in checking it or rendering its disappearance more rapid than ordinarily when antitoxin is not given. Indeed, in the one case the father of the child thought her condition became aggravated after antitoxin was given.

In none of the twenty-four cases could any beneficial influence on the membrane be observed, in such a way as to be beyond doubt. In all of them the temperature was sent up a degree or two; the pulse was accelerated, and in some cases became irregular. In some cases the patient became exhilarated or irritable, in most cases depressed, and in others there followed no general phenomena. Several cases developed a slight diarrhoea after the injections had been given. A few complained of vague joint pains. Only one boy, three years of age, developed red, painful, and swollen knee- and elbow-joints, which lasted less than a week, and which followed the injection of the antitoxin. In this case, simultaneously with the joint affection, a papular eruption appeared over the body generally, but particularly abundant on the legs, where it finally became purulent and crusty. This eruption was preceded and accompanied by an annoying pruritus. This boy finally recovered, and without the development of any parietic condition anywhere. There was no marked albuminuria in any of the cases, either before or after

the injection of antitoxin. In some cases it was thought to have become increased after the injection, but of this I am not sure. In many of the cases the amount of urine became increased after the injection. None of these patients was rendered sickly and ailing for any great length of time after antitoxin had been injected.

Although none of these patients died, no conclusion in my opinion bespeaking the beneficent powers of antitoxin is justifiable. Patients treated without antitoxin did just as well and were not afflicted with the minor inconveniences that may be attributed to antitoxin.

Conclusions.—1. Whatever thousands of antitoxinated cases of diphtheria may seem to prove to hundreds of other physicians, my twenty-four cases teach me clearly enough that the remedy has no well-marked favorable effect on the general or clinical course of the disease—it neither shortens nor lessens its severity.

2. In the croupous cases it exerted no beneficial or inhibitory influence on the progress of the croup. The operations in these cases, and not the antitoxin, saved the children.

3. In none of my twenty-four cases, nor in those seen in the practice of some of my acquaintances, did the antitoxin seem (beyond a reasonable doubt) to cause the pseudo-membranes in the throat to disappear sooner than would have been the case had no antitoxin been given.

4. In all of my cases the initial dose of antitoxin was given not earlier than the third day, and not later than the fourth day. None of the cases was markedly "septic" or "mixed," nor were they severe cases in any sense.

Consequently, in view of the above conclusions, which are based on practice and not on speculation, and what has just been said of the time of injection and the character of the cases—consequently, I say, antitoxin is not a specific in the treatment of diphtheria.

One more word in conclusion. Drs. Biggs and Guerard, in their very lengthy summary of "Antitoxin Serum in the Treatment of Diphtheria,"¹ quoted with apparent unction and much applause the following rhymes:

"The best critics in the world are they
Who along with that which they gainsay
Suggest another and a better way."

The sense of the rhymes, and the unctuous applause the gentlemen quoted allow them, are based on a misapprehension of what practical criticism should be. All through life we are critics, and not from choice. Criticism is judgment forced into action. As practitioners we are obliged to be critics for the benefit of our clients. And as practitioners we cease to be academic disputants, and always are judges and executors, and often expositors as well! It was not a poet in the sense of a rhymester, nor a great philosopher in the sense of a drawing-room hero, who said: "Be sure you are right, then go ahead." In this antitoxin business we practitioners have not been granted the privilege of thinking that we are right. We were treated as though we could not think and need not think. We had to accept what scientists and the public clamor they set in motion forced into our hands. We were more or less regimented: forced to do, and not to question why! And that, too, by men who it now seems really did not know, but only imagined or thought they knew.

In a subsequent essay I shall try to prove by means of statistics, constructed by others, all that my own experience has taught me and all that the above conclusions imply.

406 WEST THIRTY-FOURTH STREET.

¹ The Medical News, December, 1896.

ANTITOXIN, DIPHTHERIA, AND STATISTICS.

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I. CONCLUSIONS, however much enthusiasm they may arouse, are never stronger than the premises from which they are derived. The value of antitoxin as a specific remedy for the successful treatment of diphtheria is proved most frequently by conclusions expressed statistically. But statistics are not facts, but their envelopes. Statistics facilitate the memorizing and transportation of the results of much and complicated mental experimentation. Statistics always presuppose a good deal, because they never are elementary, but final statements of facts or supposed data. And because statistics take so much for granted, they are often so bewilderingly meaningless to the ignorant or uninitiated. They are also often alluring traps for unwary or careless and hasty thinkers to fall into. Honestly, generously, and studiously considered, statistics are profitable compounds to wrestle with. Statistics often give strength to preconceptions; and sometimes they demonstrate the unexpected.

In weighing and comparing the "antitoxin-in-diphtheria" statistics of different antitoxin advocates, and those statistics with old-time non-antitoxinized diphtheria statistics, in all instances we should strive to be sure that unlike things and conceptions are not being manipulated as though there were no existent differences and no distinctions to be noticed.

Antitoxin is no well-defined entity or substance.

It is a more or less arbitrary something, biologically, technically, and logically. In the next place, it is a pathological derivative and a poison. And, finally, its units of strength are arbitrary and irregular, which, with age and under varying conditions of temperature, are fugacious. Samples from different factories examined by competent analysts have been sometimes found "so feeble in antitoxin properties as to be practically worthless for therapeutic purposes. More of them, however, contained greater antitoxin properties than fell below the strength stated on the label."¹ The brand that may come in for a large share of praise with one friend may be damned by the next. For instance, Dr. Charles Graefe, of Sandusky, Ohio, found that "the results, both as to the apparent time elapsing between the injection and the separation of the membrane, and the mortality results," in diphtheria treated with a particular make of antitoxin, after a while were not so good as formerly; and he then asked the makers for an explanation. The merchants replied, as merchants do, that their antitoxin was up to the standard and that the trouble must be with the disease—that is to say, the disease had probably become more virulent. Dr. Graefe's disappointments were not assuaged by this stock explanation, because in his practised judgment he had given sufficiently large doses of antitoxin of that particular make, and, moreover, he had repeated his doses. He then tried another maker's antitoxin, and then he congratulated himself and the new makers on his revived and better successes. But strange is fate. This very make, which gave rise to new hopes in Sandusky,² showed itself capable of allowing one-third of the cases (in which it was given) at Philadelphia³ to die.

¹ Editorial, Medical News, December 19, 1896.

² Charles Graefe: the Toledo Medical and Surgical Reporter, March, 1898, p. 178.

³ Philadelphia Bureau of Health, Annual Report, 1897, p. 92.

All who have used antitoxin for diphtheria are not unanimous concerning its immediate effects on the system generally or on the complexion of the disease. Some say the disease is shortened; others do not concede this. Baginsky finds no marked general effect immediately after the injection, but he believes or thinks that the whole course of the disease assumes a friendlier, a calmer, a more satisfactory, and a speedier return to a normal state. Judging by what I have seen in my own practice, treating cases with and without antitoxin simultaneously, I cannot corroborate Baginsky's assertions. *En passant*, I may say that I have notes of three cases of naso-pharyngeal and tonsillar diphtheria, one of them croupal, which needed no medical attention after three and (in two cases) four (successive days) visits. And no antitoxin was used. The clinical diagnosis was corroborated by the health-board bacteriologist.

When five hundred, or seven hundred, or fifteen hundred, or twenty-five hundred units of antitoxin are given to a patient, the difference of dosage does not manifest itself by any recognizable or specific sign of a favorable character, but sometimes unwished-for evidences of its use present themselves, in the way of joint pains, rashes, pruritus, cardiac irregularities, increased temperature, etc.

From the foregoing statements and those found in my two preceding papers, we may formulate the following elementary conclusions concerning antitoxin as a mercantile commodity, and regarding its immediate effects on the system afflicted with diphtheria:

1. It is a substance and a remedy of variable and irregular "unit" strength.

2. The same make of antitoxin may reap fulsome praise at one place, and at another place damn itself with a large mortality rate.

3. Antitoxin is an organic substance, which is easily rendered inutile by age and unfavorable tempera-

tures (it sometimes deteriorates in spite of good handling).

4. In comparing and weighing statistics which claim to prove the potent beneficence of antitoxin, we should not forget that antitoxin and diphtheria are not two conceptions that fit one the other like nut and screw. Antitoxin is as fickle and uncertain, as merchandise and as a remedy, as diphtheria is at different times and places a variable disease complexion. In neither case are we dealing with fixed and rigid standards and certainties.

II. Has antitoxin any marked influence on the pseudo-membranous deposition, inhibiting it or hastening its disappearance? Serum advocates usually say, "Yes! most decidedly." How do they prove it? They say in two or three days after the serum has been injected the pseudo-membrane begins to disappear or has done so. And then they jubilantly tell us that is about one-half the time that it takes non-serumized cases to get rid of the pseudo-membranes.¹ Baginsky gives the membranes three or four days to disappear—also earlier, he says, but also later; that is, the sixth or seventh day after the injection of serum.² A friend of mine has reported a case in which, in an adult, the membrane persisted for several weeks, although antitoxin had been used several times. In the first antitoxin case I had the opportunity of observing, in which large doses of serum had been used, the membrane continued to grow, and the older portions did not roll up at the edges, etc., and disappear, according to the classic fashion described by antitoxin enthusiasts. Alonzo Clark, writing in 1861, says: "It is very common to observe the membrane fall off after a duration of from one to two, three, or four days—and re-form in the same place." This same peculiarity is

¹ O. Wiemer: "Das Diphtherie-Heilserum," p. 97.

² H. Baginsky: "Diph. und diph. Croup," p. 315, Wien, 1898.

seen to occur in serumized cases too. I have seen it do so in my serumized cases—form again on places where it had fallen away. I have seen this happen in cases treated by some of my friends. I have seen this re-formation of membranous deposit take place in different cases that had been treated with different brands of antitoxin. In the two dozen cases in which I used antitoxin, and in the antitoxin cases of my friends, I have not been able to convince myself that antitoxin had any marked and undoubted influence in either checking the deposition and spreading of membrane, or hastening its disappearance. The membrane seems to me to develop and retrograde under antitoxin treatment very much as it does in cases that have not been treated with antitoxin. It should not be forgotten that in different cases membranes show up differently, and that different epidemics develop varying peculiarities concerning the character of the membranes, the rapidity with which they form and disappear.

It having been shown that evidence is not wanting which proves that antitoxin is evidently a remedy of irregular, uncertain, and indefinite power for good; that immediate favorable effects on the constitution of the patient do not become evident; and that, everything considered, its effect for good on the pharyngeal pseudo-membranes is *nil* in all probability—it is not unjustifiable to conclude that antitoxin, as we know it and have known it, has no power to check or mitigate diphtheritic laryngeal processes. But let us see what can be said for and against it in

III. Laryngeal Diphtheria.—A good many if not all antitoxin advocates lay special stress and emphasis on the great good that antitoxin accomplishes in laryngeal diphtheria. What many antitoxin enthusiasts mean by laryngeal diphtheria and croup is not always clear to others. Some dignify hoarseness, cough, and indications of stridor with the diagnosis of croup.

Others call cases croupal when there are laryngeal spasms and obstructed laryngeal respiration, and cyanosis to some extent. Jenner¹ taught that "membranous inflammation of the larynx is one of the gravest diseases; it kills rapidly. If the termination be fatal, it usually is so within a few days from the outset; rarely does the disease last a week, supposing the windpipe has not been opened." This same excellent observer says: "I have never known laryngeal symptoms (due to diphtheritic pseudo-membranous deposition) commence after the first week of the disease. In rare instances death may occur within twelve hours from the time that laryngeal symptoms are first noticed. Some cases may last five days." And "rather more than half the fatal cases of diphtheria" he had seen resulted directly from disease of the larynx.² Thus the conception croup is an elastic one. Croupal symptoms are not always caused by pseudo-membranous deposits in the larynx. (Edema above, or below, and between the vocal cords is a frequent cause. And, however anxious croupal symptoms may make us feel in the start, they soon ease our anxieties or increase our apprehensions of worse things to follow. Bearing all this in mind, we are apt to shake our heads when we are told that "over one-half of all laryngeal cases³ (of diphtheria) treated with antitoxin recover without operation," and we say, "a consummation devoutly to be wished."

Assertions like this one of Caillé's have no general applicability or value, although they are true enough to arbitrary definitions and to particular personal experience and practice. But arbitrary definitions and particular personal experience, however ample and important, are insufficient to settle questions like

¹ "On Fevers and Diphtheria," 1849 to 1879, p. 565.

² *Op. cit.*, p. 516.

³ August Caillé, M.D.: "The Modern Treatment of Diphtheria." Reprint from the Post-Graduate, p. 16.

those connected with laryngeal diphtheria. These questions are settled largely by means of statistics, and statistics simulate but the last stroke of the hammer that breaks the rock. They imply so much, and take so much for granted.

Caillé's assertion has statistical foundation, and his assertion implies several conclusions which can or cannot be substantiated by statistics.

1. If antitoxin be the specific it is claimed to be, it should diminish the number of croup cases every time and everywhere. And diminishing the number of croup cases also implies the diminution of the relative number of croup operations—relative to croup cases and to cases of diphtheria all told.

2. If antitoxin be the specific it is claimed to be, epidemic influences should become scarcely noticeable in antitoxinized cases; at least the great differences and variations noticed in non-antitoxinized statistics should become very much minimized in those antitoxinized.

Baginsky, in a series of 799 cases of true scientific diphtheria observed in the course of three years, says there were 258 cases of laryngeal stenosis. Twenty-two of these were diagnosed as being simply catarrhal in character. One hundred and thirteen of true croup got well without operation, and this agreeable result is attributed to antitoxin. Six patients died of "sepsis," and on them no operation was attempted. One hundred and ~~eight~~ ^{nine} cases ~~were~~ ^{recovered} operated upon; ninety-four were intubated; four were tracheotomized; and seven were tracheotomized after intubation failed. } x

Do not Caillé's claim and Baginsky's figures alongside of Jenner's teaching make us conclude that different teachers and observers are guided by different conceptions?

Many writers, especially those who wrote before antitoxin was a commodity and bone of contention, conceive croup in Jenner's sense, and, in writing of

Should read: 105 cases of those operated recovered; 94 intubations; 4 tracheotomies, and 7 tracheotomies after intubation failed

croup, treat only of the operative cases. Croup cases that get well may be happily left to themselves, and then for our particular purpose they will give rise to no misunderstanding and dispute. In what follows we shall compare only croup cases that called for operation, those which were serumized and those which were not serumized. Of Baginsky's 799 cases of diphtheria, 15.39 per cent. though serumized, demanded operative relief; and the mortality of these croup cases, though serumized, was no less than 32.38 per cent. Allowing our trained imaginations to play with Baginsky's other figures, we conclude that the type of his diphtheria as a whole was somewhat better or more favorable and milder than the type of diphtheria that Dr. Welch dealt with in 1897 at Philadelphia, in the Municipal Hospital. Dr. Welch says: "The proportion of deaths among laryngeal cases requiring operation was considerably larger (in 1897) than in any year since 1894. The number that required intubation was 182, and of these 127 died, making a death rate of 69.78 per cent., as against 60.25 per cent. in 1896, and 54.91 per cent. in 1895." (In all these years antitoxin was used, but in none of them so thoroughly as in 1897.) Of these 182 cases, 167 received antitoxin and 115 of them died, making a death rate of 68.86 per cent., as against 56.06 per cent. in 1896, and 52.94 per cent. in 1895. Welch does not give the whole number of croup cases; but 16.81 per cent. of all the whole number of serumized cases (993) had to be intubated. When we compare Baginsky's figures with those that Welch gives, we see that, although the Philadelphia diphtheria had been getting worse, in the number of cases needing operation in the judgment of the respective men the difference of only 1.42 per cent. existed. Their general and their operative mortalities differed a good deal more. Baginsky's general mortality was only a little over 9 per cent., and his operative mortality, as already stated, was 32.38 per

cent. Welch's general mortality was 26.28 per cent., and his operative mortality was 68.86 per cent. Both observers report results influenced by serum-therapy, and yet what a difference! Just about as many cases proportionately to the number of patients with diphtheria needed operation, but only half as many died at Berlin as died at Philadelphia. What is this difference of thirty-six per cent. in operative results due to? Certainly not to technical ability. Probably not to antitoxin potencies. Possibly, to some extent, to a difference in the run of cases. But, most of all and mainly, to a difference in the type of the disease as respects severity and the complexion of pathological processes, and other reasons which our imaginations are ready to explain, but concerning which it is best to say nothing about. One fact, however, which these German and American figures make evident, and which it is proper to direct attention to in passing, is this: When the general mortality is low, the operative mortality will be low also, and *vice versa*. This fact or law is evident in non-serumized cases too. Thus at Zürich, in 1883-84, the general mortality for diphtheria was eleven per cent., and for tracheotomy in croup, forty per cent.—a mortality much better than Welch's serumized mortality for intubation, and no worse, on the whole, than Baginsky's intubations and tracheotomies. In 1889 (at Zürich) the general mortality for diphtheria was thirty-one per cent., and for croup tracheotomies, eighty-three per cent.¹

Serumized cases of tracheotomy for diphtheritic croup vary as widely in mortality percentages in hospitals treated in London at the same time as intubations do in hospitals located in cities as far apart as Berlin and Philadelphia, in different though successive years. In London,² in the six hospitals of the metro-

¹ Martin Neukomm: "Die epidemische Diphtheria, etc., in Canton Zürich," p. 57. Leipzig, 1886.

² Report for the year 1896, p. 30.

politan asylums board, 197 tracheotomies were done in cases of diphtheria that had been serumized, and 80 of them died—a mortality of 40.6 per cent. The general mortality for diphtheria was 25.9 per cent. The lowest mortality for tracheotomies of the six hospitals was 24 cases, 7 deaths—29.1 per cent. The general diphtheria mortality here was 19.7 per cent. (Fountain Hospital). The highest tracheotomy mortality—38 cases, 24 deaths—was 63.15 per cent. The general diphtheria mortality was 21.80 per cent. (Western Hospital). And all these tracheotomy cases had been serumized! Alongside of these serumized tracheotomies place the following tracheotomy statistics which are innocent of sero-therapy. Kohts reports from the Strasburg Hospital ¹ forty-four tracheotomies and eleven deaths—a mortality of twenty-five per cent. The general diphtheria mortality was only six per cent. Suppose that had been a serum year! This is another illustration of the law that a low general mortality allows a low operation mortality. A. Jacobi has told that from 1872 to 1874 he had fifty consecutive tracheotomies for croup, and all of them died. On the other hand, Drobrink had, in the course of five and one-half years, one hundred and seventy-six tracheotomies—no serum used—and a mortality of only thirty-seven per cent. At Zürich, in 1884, the mortality for tracheotomies was twenty-nine per cent. And now to end up our tracheotomy instances with secondary tracheotomies in serumized cases: At the Hôpital Trousseau, Paris, in 1897, where the epidemic has been about as favorable as at Berlin, in fifty-six cases where intubation failed and secondary tracheotomies were done, forty-five deaths resulted, or a mortality of eighty per cent.² Of course we willingly admit that these were tough cases, but can we overlook the little good anti-toxin exerted? And Baginsky had twenty-two trache-

¹ *Therapeutische Monatshefte*, April, 1895.

² *Monatsschrift für Ohrenheilkunde*, September, 1898, p. 429.

otomies in cases that repeated intubation failed to relieve—all serumized cases—and fifteen of them died—a mortality of 68.2 per cent. In 1892 George McNaughton¹ tabulated seventy tracheotomies following intubation—eleven recoveries—or a mortality of 84.29 per cent. And this is not so very bad alongside of the secondary tracheotomies of the Hôpital Trousseau, and they show how inutile antitoxin is. Of course McNaughton's cases are non-antitoxinized and reported by twenty-nine physicians and surgeons.

And now a few words concerning intubation statistics in particular. Before serum-therapy was introduced, it was the effort of intubation advocates to prove that intubation in croup gave better results on the whole than tracheotomy could. It was claimed by George McNaughton² that of every hundred cases operated, six more are saved by intubation than by tracheotomy. If this is true, let the fact not be forgotten when serumized intubations are compared with tracheotomies, serumized and not serumized, in so far as their respective mortality percentages are concerned.

The American Pediatric Society's serumized intubation statistics have been fulsomely quoted and favorably commented on as proving the great beneficence and power of antitoxin in reducing the mortality rate everywhere in Europe and America. They have been pointed to and utilized over and over again in the way of argument, as though they were elementary, ultimate, and indubitable facts. And yet what do they amount to? It has been said: "The fact that these statistics were drawn from different and widely separated localities, and therefore under every possible variation as to local conditions, severity of epidemic, etc., gives them a value much greater than that of statistics shown from single institutions, and effectually

¹ "Treatment of Croup by Intubation of the Larynx," tables.

² *Op. cit.*, 1892, p. 26.

answers the argument that the favorable results of the use of antitoxin are due to the mildness of epidemic, inclusive of a large number of mild cases owing to report of Klebs-Loeffler bacillus, special facilities for antiseptic treatment, etc." This is not mixed metaphor, but it is a mixture of fact and not fact, and so much so that the whole paragraph is void of sense. To collect its data, the American Pediatric Society sent out thousands of circulars, and only 615 physicians recorded their experience in only 3,384 cases. And to these cases were added 942 and 1,468 cases respectively treated at their homes by the New York and Chicago boards of health. The mortality was 713 deaths—12.3 per cent. The above paragraph quoted to the contrary, epidemic influences and the Klebs-Loeffler bacillus have played no unimportant part in the building of the American Pediatric Society's statistics. And the factors summarized as "human nature" have in the opinion of many practitioners contributed a vitiating quantity to the compounding of these statistics, not only by what went into them but also by what remained out of them. And then the health board additions demand a modicum at least of what has been called worldly wit to interpret them in such a way as to make them fit the probable natural facts and not interested considerations.

To go on with the American Pediatric Society's report: In one-half of the laryngeal cases intubation was not required. That fact is unimportant, because of its elasticity. It is important to know that of 537 cases of laryngeal cases demanding operation, 25.9 per cent. died. Intubation is presumed to have been the operation in all cases. We have here a low general mortality for diphtheria, and consequently a comparatively low operative mortality. Each physician reporting these cases had an average field of observation of only between five and six cases, and not a whole operative case. Everything considered, the average field

of observation is a very meagre one; and the collective whole or composite picture which results is a rather blurred water-color. It lacks definition and finish, because the results obtained and the conclusions based on these are compared only with the worst that has happened, and not with the favorable aspects of diphtheria results and statistics of former times. The American Pediatric Society's final findings are not so good as Baginsky's quoted intubations by sixteen per cent., and better than the intubation percentages of Welch by thirty-four per cent. Such differences, and serum was faithfully and carefully used in every instance!

To show to what false conclusions limited views can lead, Dr. McCallum may be quoted. McCallum tells us that "in the Boston City Hospital, during the year ending October 31, 1896, there were two hundred intubations (serumized), with a fifty-three-per-cent. mortality rate."¹ He says that many of these cases were moribund. And further to mitigate this large serum mortality, we are told that the intubation mortality of 1895 was eighty-three per cent., a difference of thirty per cent. in the two years—and this betterment is attributed to the influence of serum therapy as the only possible explanation. Such thinking strikes one as rather electrical, when we know that in the history of diphtheria even greater differences and contrasts have occurred between two successive years, when no antitoxin was used. Thus in Zürich, in 1883, out of fifty-four tracheotomies forty-one died—a mortality of seventy-six per cent.; while during 1884, out of thirty-eight tracheotomies, comparatively speaking, only thirteen died, or a mortality of twenty-nine per cent.—a difference of forty-seven per cent.

It would be easy to multiply instances to prove the

¹ Boston Medical and Surgical Journal, December 31, 1896, p. 676.

points I have been trying to make clear, but nothing would be gained thereby. Life is short and the MEDICAL RECORD space limited, and this essay must be kept within reasonable bounds.

Remembering that croup in diphtheria is an early complication, usually secondary to nasal and pharyngeal disease, and that croup cases call for operation between the second and seventh or eighth day of the disease most frequently; and remembering, furthermore, that antitoxin, to be most effective, should be administered during the first three days of the disease, and to be effective at all before the seventh or eighth day, it would seem to be a good test as to its effectiveness if the length of time during which the tube must remain in the larynx were evidently indisputably shortened. In these cases the disease and complication of croup are most active during the time that the antitoxin is supposed to develop its greatest antitoxic virtues. This is the condition most fitted for the grand remedy to win honors. And the proof would be, as already stated, lessening in an unmistakable manner the length of time that a tube must remain in the larynx or a cannula in the trachea.

In 1896, Dr. Joseph E. Winters, with the boldness of a clear-sighted and fearless clinician, asked the fair and pertinent question: "If antitoxin does not cause a 'melting away' of the membrane, and does not lessen the duration of the membrane in the visible portions of the throat, what reason have we for supposing that it influences the duration of the membrane in the larynx?"¹ It has been claimed by Bokai that, because of the liquefying effect of the antitoxin on the laryngeal diphtheritic processes, the intubation tube can be removed about eighteen hours sooner than used to be the case. This would not be a great gain, and the assertion is based on a too limited basis.

¹ "Clinical Observations upon the Use of Antitoxin in Diphtheria," etc. Reprint, p. 46.

What are the facts on a broad and time-extended basis, and all other influences allowed for?

In 1892 George McNaughton¹ said: "The proper time for the removal of the tube is a point to be decided by the operator; the average time will be about five and one-half days, but I have not been in the habit of determining by time, preferring to wait until the disease has stopped and the diseased tissues have taken on healthy action, as indicated by the cleaning of the tongue and other signs that are expected in convalescent patients." Baginsky says that the tube was allowed to remain in the larynx in pre-antitoxin days, as a rule, six and seven days. Here we have a difference of from one-half to one and one-half days as to the average time during which circumstances necessitated the lodgment of the tube in the larynx in diphtheritic croup when antitoxin was unknown. But in antitoxin cases O. Wiemer² teaches that the tube may be taken away on the third day after operation in intubation. Baginsky, in serumized cases, makes it the fourth day. Here, with two enthusiastic antitoxin teachers, we have an optimistic difference of twenty-four hours at least. In one of my cases in which the diphtheritic process was rapid, in a five-year-old girl, the tube being inserted on the first day of the croup and the second day of diphtheria, and into whom about 3,500 units of antitoxin had been injected within the first forty-eight hours of the disease, the operator thought it well to let the tube remain in the larynx for one week. Here was a case that certainly should have corroborated the rule laid down by Wiemer or Baginsky: rapid disease process, early croup complication, and sufficient antitoxin within the first twenty-four and forty-eight hours of the disease; but

¹ "Treatment of True Croup by Intubation of the Larynx." Reprint from the Brooklyn Medical Journal, p. 5.

² "Das Diphtherie-Heilserum," p. 100. Leipzig, 1898.

the disease remained and continued indifferent to the antitoxin.

Tracheotomy is, on the whole, a less favorable operation than intubation, and yet Solis Cohen¹ tells us that in occasional instances the cannula may be removed on the first day after operation. And this was at a time when sero-therapy was unknown. In other instances decannulization could not be accomplished until a week or two after operation. But the usual time was, for decanulement, between the fifth and ninth days. Sanné found it possible to remove the tracheal cannula before the end of the eighth day in sixty-one cases out of one hundred and eight tracheotomies.² And Neukomm reports, from Zürich, that in eighty-one recoveries from tracheotomy the cannula was removed on the fourth day after operation in four cases; on the fifth day in twenty-one cases; and on the sixth day in sixteen cases.³

Not only do individual peculiarities count in this matter, but the epidemic type most of all. Baginsky's cases seem to me not to have been of an extraordinary or severe type. The severity as well as the frequency of croup are in all probability beyond the control of any remedy we know of, in the sense and to the degree that Baginsky and others would have us believe. In one case of mine that had been well serumized—or was at the time so considered, with more than two thousand units—a four-year-old boy—and then tracheotomized, I was obliged to retain the tube seven days. When we consider that McNaughton's average time of extubation was about the fifth or sixth day after operation in cases where the mortality was sixty to eighty per cent., and Baginsky's average time on the fourth day after operation in cases whose mortality was only nine per cent., which indicated a mild type of diph-

¹ Solis Cohen: "Croup in its Relation to Tracheotomy," p. 59 Philadelphia, 1874.

² Solis Cohen: *Op. cit.*, p. 59.

³ *Op. cit.*

theria, I fail to be able to pronounce in favor of antitoxin when extubation and decanulement are concerned.

IV. Mortality Statistics.—The foregoing remarks and facts are only a very small portion of all facts and interpretations of them that relate to the topics discussed; but they present the facts fairly and in quantity sufficient to justify the opinions expressed and conclusions emphasized. The conclusions are that antitoxin does not check the disease or limit its time duration, and that it has no influence of a material and self-evident character on the local pharyngeal process or on the croup complication. This being so, antitoxin might, in some way not evident to crude clinical observation, exert such influences on the constitutions of patients and the diphtheritic processes going on in them, as would lessen the mortality rate in a manner that could not be misunderstood or doubted and denied. Does it? What do statistics say? Generally stated, epidemics of diphtheria have prevailed that have killed as few as two to five of every one hundred of its victims, before antitoxin was in vogue. And there have been times when as much as fifty and ninety per cent. have succumbed to it. Diphtheria is the most erratic of infectious diseases. Its mortality rate differs at different places at the same period of time. We find that diphtheria has been spreading in London and increasing its mortality rate from 1885 to 1894 (inclusive) thus:

Year.	Deaths from Diphtheria.	Year.	Deaths from Diphtheria.
1885.....	896	1890.....	1,417
1886.....	846	1891.....	1,361
1887.....	953	1892.....	1,885
1888.....	1,311	1893.....	3,265
1889.....	1,616	1894.....	2,670 ¹

¹ Pages 34, 35, Twenty-fifth Annual Report of the Health Department of the City of Boston, Mass., for 1896.

During this period the death rate for diphtheria has been lessening at Paris, France; and at Berlin it has, when not stationary, lessened. Or take Zürich, from 1879 to 1884, during which time the morbidity increased from 834 cases of diphtheria in 1879 to 1,562 in 1884, and the death rate diminished from thirty-one per cent. in 1879 to eleven per cent. in 1884; thus the sick list almost doubled, and the death rate became two-thirds less! ¹ At Hamburg, Germany, the number of sick with diphtheria at one time diminished, but the number of deaths due to the disease increased. ² And Wunderlich tells us that sometimes older children and adults are preferably attacked by diphtheria; whereas usually it is a disease commonest and most fatal in children under five years old. These facts, and facts like them or similar, must not be overlooked in all considerations that deal with particular conclusions or groups of statistics bearing on serumized or unserumized mortality statistics.

To begin: Dr. J. Febiger (Copenhagen) reports, from May 13, 1896, to May 13, 1897, that 484 patients having diphtheria and croup were admitted into the hospital. Those admitted on one day were serumized, and those coming the next day were treated without serum. Those treated with serum, 239 cases, had a mortality of only three per cent.; and those treated without serum, 245 cases, had a mortality of twelve per cent. ³ — a difference of nine per cent., which, when everything is considered, is not very great. I have a letter before me from Dr. William M. Welch, of Philadelphia, in which he gives notes of an epidemic of diphtheria affecting the students of Girard College in that city. He says: "During this

¹ Neukomm: *Op. cit.*, p. 37.

² Arthur Newsholme: "Origin and Spread of Pandemic Diphtheria," p. 109. London, 1898.

³ Internationales Centralblatt für Laryngologie, etc., Jahrgang xiv., No. 11, p. 547.

prevalence of the disease there were in all one hundred and twenty-one cases, with three deaths. Five of the cases received antitoxin, and the three deaths occurred among these. Among the one hundred and sixteen cases which did not receive antitoxin, no deaths occurred. It is fair to state that the ages of the children in Girard College range between seven and seventeen years, and, as you know, age has much to do with the death rate in any series of cases. The disease was in good part mild, yet there was a large number of severe cases." Do not these two instances, put in juxtaposition, in many respects neutralize any argument in favor of antitoxin?

Now turn to the Municipal Hospital of Philadelphia. During March, 1896, 44 cases of diphtheria were treated with antitoxin; 18 died, giving a mortality of 40.9 per cent.; but during October 126 cases were treated with antitoxin, 21 died, and the mortality was 16.66 per cent.¹ Here is a mortality difference of no less than 24 per cent. in a spring and an autumn month in the same hospital in the same year. And then there is Professor Hennig, who lost only 59 cases of diphtheria in a total of 1,927 gathered in the course of eighteen years, or a mortality per cent. of 3.06, and this without antitoxin.²

So far figures show that antitoxin runs a lame and halting race. And yet Baginsky feels himself justified in teaching that, in so far as prognosis is concerned, the cases treated with antitoxin are as much more certain of getting well than non-serumized cases of diphtheria, as cases of varioloid are than smallpox.

Let us see whether the day of administration of antitoxin will clear up matters to justify Baginsky's varioloid analogy. Here are two tables showing the

¹ Annual Report of the Bureau of Health of Philadelphia for 1897, p. 92.

² Verhandlungen des Congresses für innere Med., 1896, p. 250.

mortalities of diphtheria according to the days of the disease on which antitoxin was given. Take Biggs' table first:¹

Day of Disease.	1.	2.	3.	4.	5 or Later.	Un-known.	
Cases treated.	44	95	73	50	62	30	344 cases = 13.2.
Deaths.....	3	11	4	6	20	3	
Mortality per cent..	6.7	11.5	5.5	12	32	10	

And now take Baginsky's table:²

Day of Disease.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	Totals.
Cases treated.....	96	240	139	111	64	26	22	28	24		750
Deaths	1	5	8	23	4	5	6	4	4		60
Mortality per cent..	1.07	2.08	5.7	20.7	6.9	19.2	27.2	14.2	16.6		8

Neither of these tables includes any moribund cases. Now notice the mortality percentages in both tables on the corresponding or like days of antitoxin administration. Biggs' table shows that of 44 cases that had antitoxin given them on the first day of the disease 3 died, or a mortality of 6.7 per cent. Baginsky's first day gives us 1 death in 96 cases, or a mortality of only 1.07 per cent.—a difference of over five per cent. The second day gives Biggs a mortality of 11.5 per cent., Baginsky 2.08 per cent.—a difference of about nine per cent. Why should antitoxin treat Baginsky with so much more favor on these most favorable antitoxin days than Biggs? On this second disease-day of antitoxin administration, the mortality difference between Baginsky's and Biggs' mortalities is fully as great as the mortality rates or percentages of Fibiger's quoted serumized and non-serumized cases. These figures

¹ "Health Department Report on Antitoxic Serum in the Treatment of Diphtheria." Reprint from the Medical News, p. 6.

² Baginsky: "Weitere Beiträge zur Serumtherapie, etc.," pp. 6, 7. Stuttgart, 1898.

speak for themselves. On the third disease-day Biggs' antitoxin mortality drops almost on a line with Baginsky's—5.5 per cent. and 5.7 per cent. But when the fourth day is tackled, Biggs' mortality advances to 12 per cent., and Baginsky's to 20.7 per cent.—a difference of nearly 9 per cent. in favor of New York. And in the enthusiasm of their "will to believe," we have had New York sero-therapists frighten us into the belief that after the third day of the disease antitoxin will fail to show up agreeably.

We must now leave Biggs to his fate, with 32 per cent. mortality for fifth and later-day cases. But we continue with Baginsky's table. Absurdly enough, and it may be provoking too, his fifth-day injections give a mortality of only 6.9 per cent., which is not much worse than his and Biggs' third-day injections, and is better by 14 per cent. than the fourth day. Antitoxin is a good deal of a flirt. On the sixth day it gives a 19.2 per cent. mortality, and on the seventh 27.2 per cent., and then on the eighth day drops to 14.2 per cent. We need do no more addition and subtraction. Biggs is jubilant with a general mortality rate of 13.2 per cent., and Baginsky congratulates himself with an eight-per-cent. general mortality.

Kohts, of Strasburg, concludes from his experience that cases injected with serum on the first and second days of the disease result in no better mortality rate than non-serumized cases do which come under proper medical care on the first and second days of the disease.¹ After these figures have been looked over and compared, have we not more than sufficient reason to ask: How much swing do antitoxin advocates wish granted to themselves, and yet have us believe that they are maintaining a just equilibrium?

What Kohts has found, that cases treated without antitoxin and coming under medical care on the first and

¹ *Therapeutische Monatshefte*, April, 1895, p. 190.

second days of disease do as well as serumized cases, I have heard men here say who have been practitioners for thirty and forty years. Cases treated after the third day with serum turn out very unequal mortality percentages, as the quoted tables from Biggs and Baginsky show. All of us who can claim only an ordinary experience with diphtheria for from ten to twenty years know that we feel more hopeful of and for our diphtheria cases, even when they are more than mild or even severe, when we begin to see them early; and after treating them for five or six days and finding croup and other complications not progressing, we begin to feel pretty sure of a favorable termination. Therefore, when the most favorable disease-days for the administration of antitoxin turn out no better mortality statistics—not in one but in all places and at all times—than when sero-therapy is not resorted to, why should we use antitoxin? Should we do so because the American Pediatric Society and other writers, who see things from a point of view all their own, wish us to believe and think as they do?

At a society discussion of the antitoxin question, in which I took part, a year or two ago, one of the most enthusiastic of antitoxin advocates stated that under his supervision fifty or more mild cases of diphtheria had been treated without serum, and that no deaths had occurred. And yet about this same time we find Dr. Caillé laying down the law: "The practitioner who *thinks* [the italics are his] a case is mild, and waits for severe symptoms before using antitoxin, utterly fails to grasp the situation, and will be frequently disappointed."¹ We do not hear of disappointment coming in these mild cases untreated with serum. But what do Caillé's quoted words imply? First, that there are practically no mild cases, and if there are mild cases the practitioner cannot diagnosticate

¹ Caillé: "The Modern Treatment of Diphtheria and Croup," p. 9.

them; and, second, the practitioner must not think, he need not discriminate and differentiate—all he need do is to squirt indiscriminately as “scientifically” commanded or advised, and he will be held in high estimation, and as being abreast of the times, and all else that is good and true and beautiful, *sans* will and *sans* phrase. It is one of the touches of human nature that makes the whole world kin, to get on the safe side, and medical practitioners are as wise in this respect as the rest of humanity. They will seek the safe side, but they will do some thinking, and say little or nothing, and suit their actions to the facts that present themselves to their senses and reasoning powers. When we are still exhorted not to think and not to believe, except as it is done for us, and it is thought proper and easy to jolly us with such half-truths as “Probiren ist besser als studiren” (trying is better than studying), as though the trying without studying were worth anything; and the Hunterian witticism, “Try, young man; don’t think,” is flung at us with supercilious condescension—and all this done in the solemn name of science and officialism—we cannot help thinking that such science is a new superstition or an old one masquerading, the supposedly long-dead “*Authoritätenglaube*.” And all this being so, we have cause to thank our stars that Joseph E. Winters, Lennox Browne, Kassowitz, Adolf Gottstein, and others have had, and still have, the courage and public spirit to protest against this “authority-faith” in public, when the public bowed to it, and believed much and did not think, and willing allowed itself to be done by it.

Conclusions.—1. Antitoxin is not always and uniformly of certain and fixed unit strength; and even when it is supposed or believed to be so, it fails to mitigate the evil mortality rates of diphtheria.

2. The differences in mortality rates or percentages vary as much in different places and at different times

among antitoxin cases as they do among cases that have not been antitoxinized.

3. Antitoxin has not diminished the relative number of croup cases that call for operation; nor has it diminished the mortality rates of operated cases, all facts, conditions, and disease-type differences considered.

4. At the present time, at certain places, the general mortality rates are low, and consequently the operative mortalities for croup are also low. At other places where the general diphtheria mortalities are high, so too are the operative mortalities high—whether antitoxin has or has not been used.

5. Allowances being made for the milder type of diphtheria that is prevalent, not everywhere, but at most places, it does not appear evident that the time during which the tracheal cannula or O'Dwyer tube must remain in the trachea or larynx, as the case may be, after croup operations, has been lessened by antitoxin therapy.

6. Antitoxin is a toxic agent in the human economy, which in the vast majority of instances in which it is given produces effects that are so evanescent as not to be noticed, and in many instances gives rise to disquieting pruritus, dermal eruptions, arthralgias, cardiac irregularities, diarrhœas, etc., and is in exceptional and very rare instances followed by death; but as a therapeutic agent it is a rank failure, despite all the hopes it enkindled and the assumption of scientific infallibility in its favor.

SIGNS OF THE TIMES

“The enthusiastic way in which some regard Antitoxin becomes at times absurd. Only the other day, a practitioner in a neighboring village, who had used Antitoxin a few times, said to me: ‘Doctor, there is but one thing to which I can compare it, and that is to the time when our Saviour was on earth, and healed the sick by His touch.’ Yet across the street from him, his fellow-practitioner had used it in four cases, and lost them all. As for myself, I am unconvinced. I have never used it.”

—A CORRESPONDENT FROM WEST VIRGINIA.

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